Effects of Local Anesthesia and General Anesthesia on Serum Levels of IL-4, IFN-Γ and IL-18 in Elderly Patients with Lung Cancer

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Abstract: Objective: To investigate the effects of local anesthesia and general anesthesia on serum levels of interleukin-4 (IL-4), interferon γ (IFN-γ) and interleukin-18 (IL-18) in elderly patients with lung cancer. Methods: 82 elderly patients with lung cancer were selected from January 2016 to August 2017 in our hospital. They were divided into general anesthesia group (41 cases) and local anesthesia group (41 cases) according to different anesthesia methods. The general anesthesia group received general anesthesia, and the local anesthesia group received local anesthesia. The changes of serum IL-4, IFN-γ and IL-18 levels before and after skin incision and after operation were compared between the two groups. The preoperative 1d, postoperative 3d, postoperative 7d cognitive function improvement, and the incidence of adverse reactions were compared. Results: two groups of skin incision and postoperative serum IFN-γ in patients with immediate gamma and lower the level of IL-18 (P<0.05); the observation group at skin incision and postoperative patients with lower level of serum IL-4 (P<0.05), and the control group at skin incision and postoperative serum IL-4 levels in patients with no significant change (P>0.05); the observation group cut skin surgery and serum level of IL-4 was higher than the control group, while the IFN-γ and IL-18 levels lower than the control group (P<0.05). The control group 3d after surgery and postoperative 7d score decreased in patients with MMSE (P<0.05); no significant changes in 3d and 7d after operation in patients with MMSE scores of the patients in the observation group (P>0.05); the patients in the observation group 3d and 7d after operation in patients with MMSE score higher than the control group (P<0.05). The incidence of adverse reactions in the observation group was lower than that in the control group (P<0.05). Conclusion: local anesthesia can significantly improve the level of serum IL-4, reduce the levels of IFN-γ and IL-18 in lung cancer of elderly patients, and help to enhance the anti-inflammatory ability of patients with lung cancer, and has important research value.

Keywords: local anesthesia; general anesthesia; elderly lung cancer; interleukin-4; interferon-γ; interleukin -18

1. Introduction

Lung cancer is a common malignant tumor, and its morbidity presents the rising trend. It is common for old people, because respiratory function of old people degrades and environmental degradation leads to the rising trend of lung cancer incidence rate [1-2]. At present, the surgery is considered to be a main treatment method. For the old patients, anesthetic dosage is relatively large so that the whole surgical process is irritant to them so that immunity of the old patients decreases and cognitive disorder may occur easily [3-4]. In recent years, the researches and reports have shown that different anesthesia methods can lead to different impacts of inflammatory factors [5]. The impacts of intraspinal anesthesia and general anesthesia on serum interleukin-4 (IL-4), interferon-γ (IFN-γ) and interleukin-18 (IL-18) of old patients with lung cancer are explored as below:

2. Data and Methods

2.1. Clinical Data

82 old patients with lung cancer who were received and treated in our hospital from January 2016 to August 2017 were chosen, and they were verified by cytology or pathology. They were classified into general anesthesia group (41cases) and intraspinal anesthesia group (41 cases) according to the anesthesia methods. In the general anesthesia group, there were 28 male patients and 13 female patients, with the age of 65~83, average age of 74.92±4.56, mean BMI of (21.94±2.35)kg/m2, and average operation time of (129.83±15.42) min. In the intraspinal anesthesia group, there were 27 male patients and 14 female patients, with the age of 66~85, average

age of 75.81±4.61, mean BMI of (22.17±2.41)kg/m2, and average operation time of (131.07±16.81) min. The general data of both groups have comparability.

2.2 Inclusion Criteria and exclusion criteria

2.2.1 Inclusion criteria

① patients conformed to operation indications of radical resection of pulmonary carcinoma, age of patients≥65; ② audited and approved by the Ethics Committee; ④ signed informed consent form.

2.2.2 Exclusion criteria

① combined with incomplete hepatic and renal function and congenital heart disease; ② combined with gastric carcinoma, liver cancer and gynecological oncology; ③ owned taboos for operation and anesthesia; ④ mental disease.

2.3 Methods

The patients of both groups received vital sign monitoring, and peripheral vein channel was established. Besides, central venous pressure monitoring and arterial blood pressure monitoring were conducted for them.

General anesthesia group (control group): the patients received general anesthesia by trachea cannula. Anesthesia induction: midazolam (produced by Jiangsu HWA Pharmaceutical Co., Ltd., GYZZ H20031037) 0.04 mg/kg, fentanyl (produced by Yichang Renfu Pharmaceutical Co., Ltd., GYZZ H42022076) 4 μg/kg, propofol (produced by AstraZeneca S.P.A.,GYZZ H20030481)2.0 mg/kg, vecuronium bromide (produced by YiChang Renfu Pharmaceutical Co., Ltd., GYZZ H20133079)0.1 mg/kg. After the patients were satisfied with muscles relaxing, trachea cannula was given, and then anaesthesia machine was connected for mechanical ventilation. Vecuronium bromide, remifentanil and propofol were used to maintain anesthesia, and BIS value of patients was monitored and controlled at 40~60.

Intraspinal anesthesia group (observation group): T6-7 gap puncture was used for epidural puncture, and 10ml 0.5% ropivacaine (Naropin, AstraZeneca) was given. When the level of anesthesia reached T2, the surgery started, and nasal catheter was used to continue oxygen uptake in the whole operation process.

2.4 Observation Indicators

(1) The changes of both groups in serum IL-4, IFN-γ and IL-18 before anesthesia, during skin incision and immediately after the operation were observed. 2mL peripheral venous blood was collected respectively and centrifuged for 10min with the radius of 15cm and speed of 2500 r/min to separate the serum which was determined within 24h. The content was determined with enzyme linked immunosorbent assay method, and the instrument is Hitachi 7600 fully automatic biochemical analyzer. (2) Cognitive function improvement of both groups 1d before the surgery, 3d after the surgery and 7 after the surgery were observed, and mini-mental state examination (MMSE) was used for evaluation. (3) The occurrence of adverse reactions was observed for both groups.

2.5 Statistical Method

Statistics software SPSS13.0 was employed for analysis. P<0.05 means there is statistical significance. The enumeration data were tested by x2 test and expressed with percentage. The measurement data were tested by t test and expressed by mean ± standard deviation.

3. Results

3.1 Comparison of patients' serum IL-4, IFN-γ and IL-18 in both groups before anesthesia, during skin incision and immediately after the operation

As shown in Table 1, before anesthesia, the difference in patients' serum IL-4, IFN-γ and IL-18 had no statistical significance (P>0.05). During skin incision and immediately after the operation, patients' serum IFN-γ and IL-18 lowered in both groups (P<0.05). During skin incision and immediately after the operation, patients' serum IL-4 level reduced in the observation group (P<0.05), while patients' serum IL-4 level had no obvious change in the control group (P>0.05). During skin incision and immediately after the operation, serum IL-4 level of observation group was higher than that of control group, while IFN-γ and IL-18 were lower than those of control group (P<0.05).

Table 1 Comparison of patients' serum IL-4, IFN-γ and IL-18 in both groups before anesthesia, during skin incision and immediately after the operation($\bar{x}$±s)

Group		No.	IL-4(pg/mL)	IFN-γ(IU/mL)	IL-18(pg/mL)
Observation group	Before anesthesia	41	10.42±1.87	2.64±0.34	248.93±13.25
	During skin incision	41	13.49±2.56*#	2.18±0.38*#	184.29±10.47*#
	Immediately after the operation	41	17.87±2.14*#	1.76±0.32*#	125.62±9.42*#
Control group	Before anesthesia	41	10.51±1.84	2.70±0.35	250.10±14.21
	During skin incision	41	9.42±1.76	2.45±0.31*	217.42±13.18*
	Immediately after the operation	41	9.35±1.54	2.09±0.27*	173.10±11.26*

Note: compared with pre-anesthesia, *$P<0.05$; compared with the control group in the same period, #$P<0.05$.

3.2 Comparison of MMSE score changes of both groups 1d before the surgery, 3d after the surgery and 7 after the surgery

As shown in Table 2, MMSE score comparison of both groups 1d before the surgery had no statistical difference (P>0.05). MMSE scores of control group 3d after the surgery and 7 after the surgery lowered (P<0.05). MMSE scores of observation group 3d after the surgery and 7 after the surgery had no obvious change (P>0.05). MMSE scores of observation group 3d after the surgery and 7 after the surgery were higher than those of control group (P<0.05).

3.3 Comparison of Adverse Reactions

As shown in Table 3, the occurrence rate of adverse reactions in the observation group was lower than that of control group (P<0.05).

Table 2 Comparison of MMSE score changes of both groups 1d before the surgery, 3d after the surgery and 7 after the surgery ($\bar{x}$±s)

Group	No.	1d before the surgery	3d before the surgery	7d before the surgery
Observation group	41	25.48±1.76	25.04±1.95	25.29±1.65
Control group	41	25.61±1.98	20.42±1.57*	22.95±1.74*#
t	-	0.3142	11.8165	6.2484
P	-	>0.05	<0.05	<0.05

Note: compared with 1d before the surgery, *$P<0.05$; compared with 3d before the surgery, #$P<0.05$.

Table 3 Comparison of adverse reactions

Group	No.	Hypotension	Nausea and vomiting	Cognitive disorder	Respiratory depression	Occurrence rate (%)
Observation group	41	0	1	1	0	4.88
Control group	41	2	3	4	2	26.83
X^2	-	-	-	-	-	7.4047
P	-	-	-	-	-	<0.05

4. Discussion

The malignant tumor will usually cause patients' autoimmune dysfunction, so operative wound and anesthesia bring about severe stress response of the body, thus leading to internal environment disturbance [6-7]. A lot of inflammatory cytokines will result in patients' excessive stress. If the balance between inflammatory cytokines and inflammatory cytokines carries important significance for host's immunity, once the balance is reached, the immunity of cancer patients will reduce. Cellular immunity of the body plays an important role for anti-tumor. Various factors in the operation period lead to immunosuppression of the body and especially damage to cellular immunity, which will further induce tumor transfer and diffusion easily [8-9]. At present, th surgery is still the main treatment method for lung cancer, but surgical stress to the body may bring about adverse reaction to the body, thus reducing immunity [10]. Helper T cell plays a very important role in immune system regulation, where Th1 and Th2 cells are two categories of Th cells. Th1 cells mostly generate IFN-γ, IL-12 and IL-2, while Th2 cells mostly generate IL-4, IL-13, IL-6 and IL-10, etc. IL-4 and IFN-γ are representative cytokines of Th2 cell and Th1 cell. In immunology, the functional status of Th2 cell and Th1 cell is known through detection of IL-4 and IFN-γ [11-12]. This study shows that serum IL-4 level of observation group during skin incision and immediately after the surgery was higher than that of control group, indicating that intraspinal anesthesia increases release of anti-inflammatory cytokines in surgical patients, enhances anti-inflammatory capacity of the body, restricts inflammatory response and thus maintains patients' immunity homeostasis. Except antivirus effect, IFN-γ also has immunomodulatory effect, activates and promotes macrophage of NK cell nucleus as well as regulates inflammatory response [13]. This study shows that IFN-γ level of observation group during skin incision and immediately after the surgery was lower than that of control group, indicating that local anaesthesia can enhance killing ability of NK cells and antitumor cells through reducing IFN-γ level, thus contributing to maintaining patients' immunity. IL-18 is a cytokine generated by mononuclear macrophage, and it can enhance inflammation protection, release histamine, enhance allergic reaction, release lyase, facilitate neutrophilic granulocyte chemotaxis and promote T cell chemotaxis and dissociation [14]. In addition, IL-18 plays a role in body immune regulation. Under normal conditions, it has multiple biological activities such as immune response regulation and participation in stress reaction [15]. The result of this study indicates that IL-18 level of observation group during skin incision and immediately after the surgery was lower than that of control group, demonstrating that intraspinal anesthesia can build up resistance.

5. Conclusion

In conclusion, for old patients with lung cancer, intraspinal anesthesia can obviously improve serum IL-4 level, lower IFN-γ and IL-18, and contribute to enhancing patients' anti-inflammatory capacity, so it has important research value.

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